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Frontal Lobe Intraconnectivity: Short-range tract characteristics in old age

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Introduction

- The frontal lobes
 - facilitate our most complex thinking
 - contain multiple cytoarchitecturally and functionally discrete regions¹
 - regions interact via complex, short-range white matter (WM) connections
- The frontal lobes are particularly prone to age-related structural decline²
- This may partially explain age-related cognitive ability decline in the elderly³
- Most studies of the frontal lobes focus on various frontal cortical areas.
- Yet, the WM connecting these regions remains relatively under-researched⁴
- It is unclear how individual differences in the number of connections and WM integrity in the frontal lobe vary in older age.

Aims

- Measure connectivity among frontal regions in older adults.
- Characterise variation in the number, density and integrity of these tracts.

Methods

Subjects & MR Imaging

- Eighty eight males from Lothian Birth Cohort 1936⁵, mean age 73.7 ± 1 yr.
- Community-dwelling, MMSE ≥ 24, HADS < 11, not on antidepressants.
- T₁W scan (resolution 1x1x1.3 mm), 1.5 T GE scanner
- DTI scan (resolution 2x2x2mm), 1.5T GE scanner

Structural Images

- Seven gyral frontal regions were manually segmented on T₁W with Analyze 8.1 using a protocol published elsewhere⁶ with excellent reproducibility (intra-rater ICCs > .96).

- Brain extraction (multi-spectral in Analyze).

- T₂*-weighted and FLAIR volumes were fused using an image fusion tool
- Brain extracted using object extractor tool
- Masks from this processes then applied to T₁W

Diffusion Tensor Images

- Motion & eddy current distortion corrected by registering all diffusion-weighted volumes to the 1st undistorted b0 image⁷

- DT-MRI reconstruction used interpolated streamline and fractional anisotropy (FA) computation in DTI Toolkit.

- Segmented frontal lobe regions then transformed to DT-MRI space (via T₁W) using FLIRT⁷

- Site-to-site connection performed in TrackVis⁸ (www.trackvis.org). Tracts connecting each pair of manually-segmented frontal ROIs were isolated.

- Primary measures were:

- Connection Probability (# tracks connecting each pair of regions / the total # frontal lobe tracks).
- Mean FA values of the connecting tracts.
- Coefficient of variation (CoV) was used to index tract variation across individuals.

Results

- Tracts (Fig. 1) and connectivity profiles (Fig. 2) concurred with previous anatomical reports of healthy younger participants^{4,9}.**
- Individual variation in connection probability and tract FA (Fig. 3) was high. Particularly for lateral and cingulate regions.**

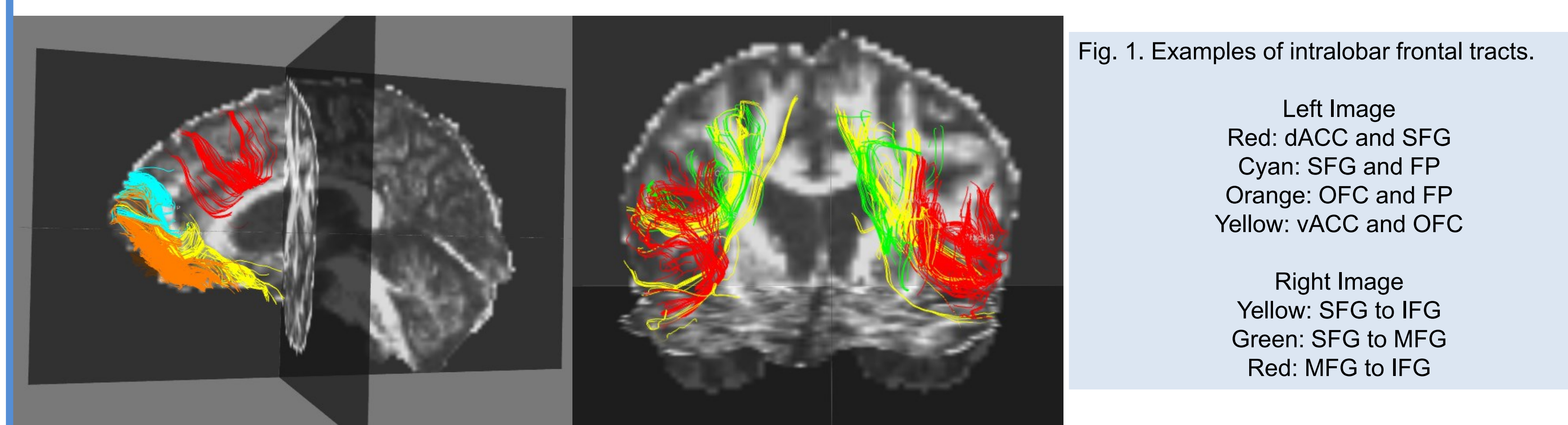


Fig. 1. Examples of intralobar frontal tracts.

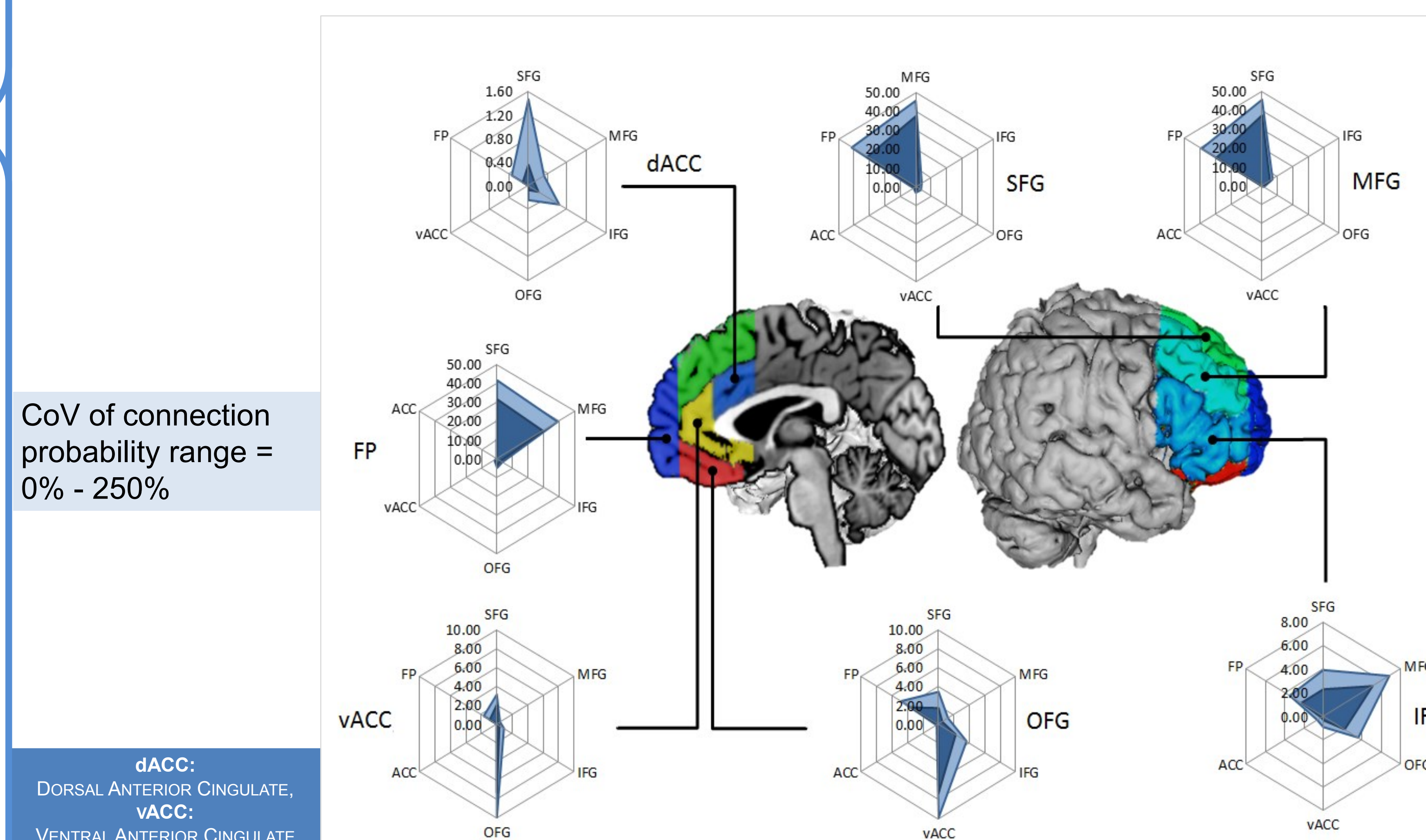


Fig. 2: Radar plot of the mean + SD (dark and light blue) connection probability (x 10²)

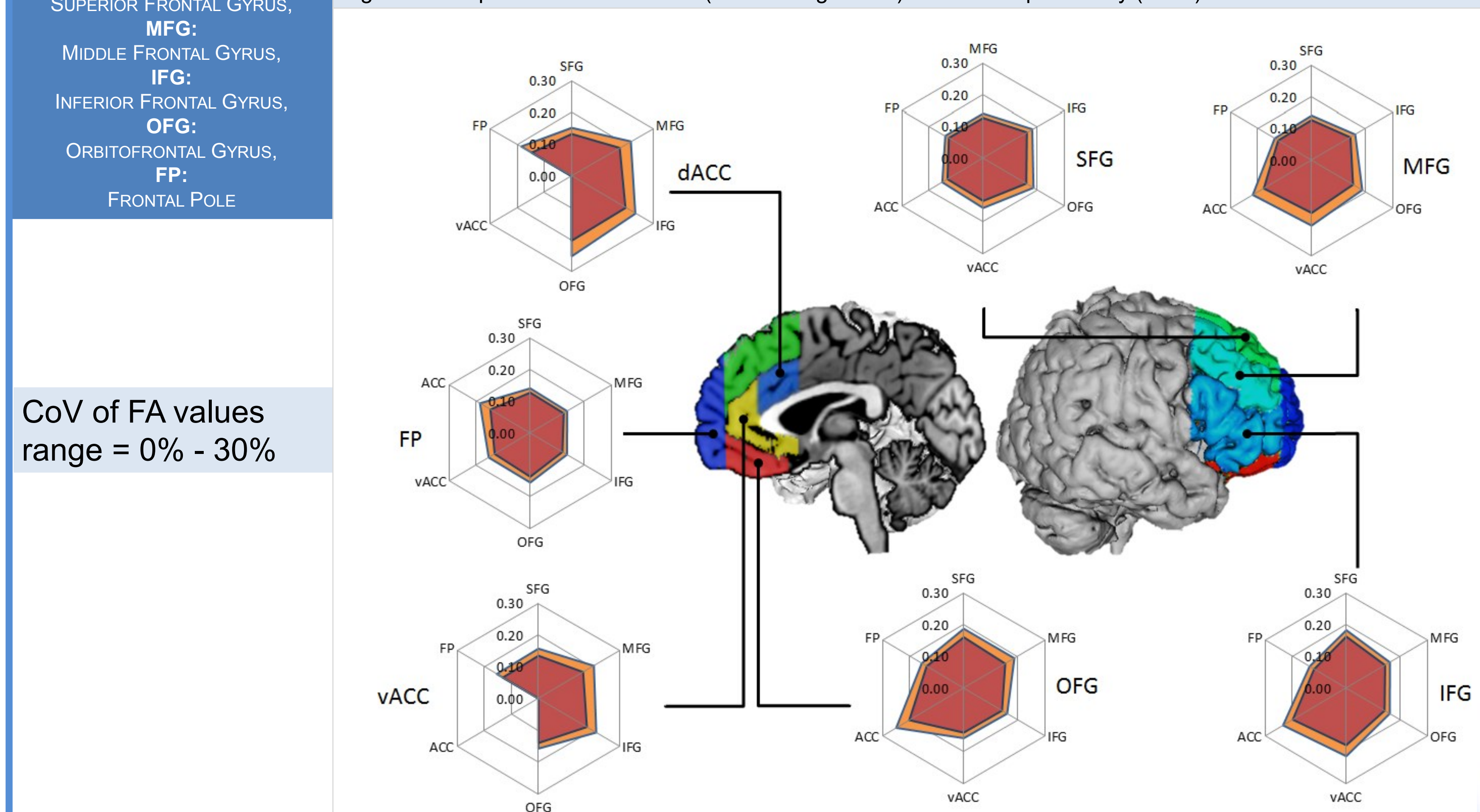


Fig. 3: Radar plot of mean + SD (red and orange) FA values of the tracts connecting frontal regions

Variation in connectivity and FA were tightly related across frontal lobe tracts ($\beta = .89, p < .000001$)

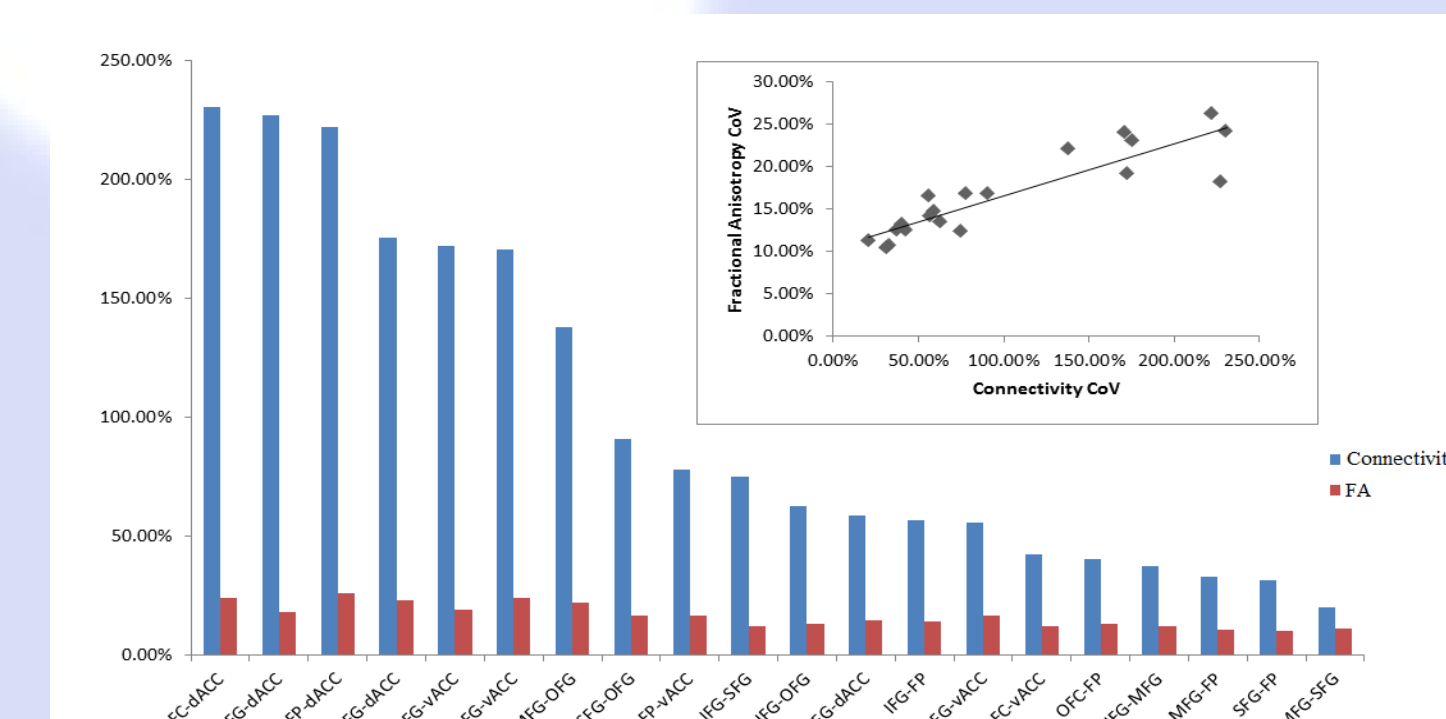


Fig. 4: Coefficient of variation (CoV) bar chart showing variability in the connection probability and FA values of the connecting tracts, and scatter plot with regression line (inset; top right) of the association between connection probability CoV and FA values CoV.

Conclusions

- The results show that the measures of connections involving cingulate and lateral frontal regions are highly variable in older age.
- This is a promising approach from which to examine the relationship between cognitive ability and the number, density and integrity of short range frontal lobe connections in old age.
- Longitudinal data or comparison with a younger group would help to determine if this variability is a feature of ageing, rather than pre-existing individual differences.
- More advanced tractography algorithms such as those based on probabilistic methods with 2 fibre populations per voxel will be investigated.

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